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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/708,786	11/08/2000	Sudhir Agrawal	47508.700	2469

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EXAMINER	
GIBBS, TERRA C	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/708,786	AGRAWAL, SUDHIR	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,8-11,14,15,17-20,23 and 29-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,8-11,14,15,17-20,23 and 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission mailed on July 25, 2005 has been entered.

Claims 28 and 35-37 have been canceled. Claims 1, 2, 10, 11, 19 and 20 have been amended. Claims 1, 2, 5, 6, 8-11, 14, 15, 17-20, 23, 14, and 29-34 are pending in the instant application.

Claims 1, 2, 5, 6, 8-11, 14, 15, 17-20, 23, 14, and 29-34 have been examined on the merits.

Response to Arguments

Applicants Amendment and Response mailed July 25, 2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed January 4, 2005 are hereby withdrawn. Any arguments addressing said rejections and/or objections are moot. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5, 6, 8-11, 14, 15, 17-20, 23, 14, and 29-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The instant claims are drawn to a method for statistically significantly potentiating the activity of an SN-38 prodrug by a p value of less than or equal to 0.08 in an unpaired t-test, comprising co-administering an oligonucleotide that is from about 5 to about 100 nucleotides in length with the prodrug. It does not appear that Applicants have support for the limitations, "a p value of less than or equal to 0.08" or "from about 5 to about 100 nucleotides in length" as recited in the instant claims.

In Applicants Remarks filed July 25, 2005, Applicants contend that support for the limitation "from about 5 to about 100 nucleotides in length" is found at page 8, lines 23-27. Referring to Applicants specification at page 8, lines 23-27, Applicants disclose preferred embodiments of oligonucleotide lengths including "from about 13 to about 100", "from about 15 to about 50", "from about 15 to about 35", and "from about 5 to about 15". However, these embodiments do not support the specific limitation "from

about 5 to about 100" as instantly recited.

In Applicants Remarks filed July 25, 2005, Applicants also contend that support for the limitation, "a p value of less than or equal to 0.08" is found in previously presented claim 38 and at pages 13 and 14. At the outset, it is noted that at no time during prosecution of the instant application was there a claim 38. Now then referring to pages 13 and 14, p is disclosed as being less than 0.08 (see page 14, line 10), but nowhere is p disclosed as being equal to 0.08.

Applicant is required to cancel the new matter or *specifically* point out the support for the limitations, "a p value of less than or equal to 0.08" or "from about 5 to about 100 nucleotides in length" in reply to this Office action.

Claims 1, 2, 5, 6, 8-11, 14, 15, 17-20, 23, 14, and 29-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for statistically significantly potentiating the activity of an SN-38 prodrug by a p value of less than 0.08 in an unpaired t-test, comprising co-administering an oligonucleotide that is from about 13 to about 100 nucleotides in length with the prodrug, wherein the prodrug is administered at a dose of 50 mg/kg and the oligonucleotide is administered at a dose of 20 mg/kg, does not reasonably provide enablement for a method for statistically significantly potentiating the activity of an SN-38 prodrug by a p value of less than or equal to 0.08 in an unpaired t-test, comprising co-administering an oligonucleotide that is from about 5 to about 100 nucleotides in length with the prodrug. The specification does not enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This is a scope enablement rejection.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the amount of direction or guidance presented, and the quantity of experimentation necessary.

The instant claims are drawn to a method for statistically significantly potentiating the activity of an SN-38 prodrug by a p value of less than or equal to 0.08 in an unpaired t-test, comprising co-administering an oligonucleotide that is from about 5 to about 100 nucleotides in length with the prodrug. The instant specification teaches that sequence independent oligonucleotides produce a statistically significant potentiating effect on irinotecan, in a dose dependent manner.

The art teaches the potentiation of antitumor activity of irinotecan by chemically modified oligonucleotides in a dose dependent manner. For example, Agrawal et al. (International Journal of Oncology, 2001 Vol. 18:1061-1069, of record) specifically disclose, "the potentiation of antitumor activity was dependent on the dose of irinotecan and chemically modified oligonucleotides administered" (see Abstract). Specifically, Agrawal et al. teach, "a dose of 20 mg/kg of chemically modified oligonucleotide and 50 mg/kg of irinotecan was found to be optimal" (see page 1068, first few lines). Further, Agrawal et al. (International Journal of Oncology, 2002 Vol. 21:65-72) teach GEM 231, a second-generation antisense agent complementary to protein kinase A RIα subunit,

potentiates antitumor activity of irinotecan in a dose dependent manner in human colon, pancreas, prostate and lung cancer xenografts. Specifically, Agrawal et al. teach, "the co-administration of GEM 231 (10 or 20 mg/kg) with irinotecan (50 mg/kg) resulted in a significant increase in mean day survival (MDS) and tumor-growth inhibition (TGI), when compared with irinotecan monotherapy" in human cancer xenograft, HCT-116 (see page 67, second column). The instant specification concurs with Agrawal et al. (2001) and (2002) at page 14, lines 10-12 where it discloses, "both Oligo 1 and Oligo 2 can potentiate the activity of Camptosar efficacy in a statistically significant and dose-dependent manner".

Assertions such as those from Agrawal et al. (2001) and (2002) in addition to self-admissions from the instant application indicate that the potentiation of irinotecan by antisense oligonucleotides is dependent on the dose of both agents.

The specification as filed and the art provide methods for statistically potentiating the activity of irinotecan with sequence independent oligonucleotides in a dose dependent manner. The instant claims do not require any specific dose of oligonucleotide or prodrug and one skilled in the art would need to practice undue trial and error experimentation to practice the instant invention over the scope claimed. The skilled artisan would need to determine the dose of the prodrug and the dose of the oligonucleotide that would result in statistical significant potentiation as claimed. These factors are not routine and the skilled artisan would need to determine such factors de novo, through empirical, undue experimentation.

Therefore, based on the breadth of the claims, the nature of the invention, the lack of specific guidance by the inventor, and the quantity of experimentation that would be required, it would require undue experimentation, beyond what is taught in the specification, to practice the methods as claimed, over the full scope claimed.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
September 19, 2005

ANDREW WANG
SUPERVISORY PATENT EXAMINER
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